Drinking Water and Health

SAFE DRINKING WATER COMMITTEE

Advisory Center on Toxicology
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data. The available data and calculations of ADI are summarized in Table VI-30.

Gas-chromatographic and thin-layer chromatographic methods are available for the analysis of diazinon in water. These methods require extraction of the diazinon from the water before analysis. Sensitivity thus depends on the size of the sample used. The anytical sensitivity of the methods, however, is adequate to detect concentrations lower than the recommended no-adverse-effect concentration in samples of reasonable size.

The data needed for the toxicologic evaluation of diazinon are fairly complete, and there is no pressing need for research to evaluate its safety. There is little information available on the actual presence or absence of diazinon in drinking-water or in sources of drinking-water. Studies on the environmental transport and persistence of diazinon would be useful in this respect.

PHORATE AND DISULFOTON

Introduction

Phorate, or *O,O*-diethyl-*S*-[(ethylthio)methyl]phosphorodithioate phosphorodithioate (Thimet R), and disulfoton, or *O,O*-diethyl-*S*-[(2-ethylthio)ethyl]phosphorodithioate (Di-Syston R), are closely related, systemic organophosphorus insecticides. The compounds differ from each other structurally only in the number of carbon atoms in the aliphatic side chain of the molecules, disulfoton having one more than phorate. Their properties and uses are quite similar. The principal uses for both compounds are in soil applications for the control of sucking insects.

There is only one report of the finding of a food containing disulfoton in the FDA's Market Basket Survey of prepared food (Corneliussen, 1970)—in a leafy vegetable containing 0.002 ppm, well below the tolerance limit. Phorate has not been found in food.

From the standpoint of total volume of use, both phorate and disulfoton must be considered as major insecticides. In 1971, 4.2 million pounds of phorate and 4.1 million pounds of disulfoton were used in the United States (NAS, 1975). Each represented 2% of the total insecticide used that year. Virtually all the phorate and disulfoton is used on crops, with less than 100,000 pounds (primarily disulfoton) being used for home and garden applications. The use of these compounds is growing steadily, with indications that further increase will occur as a result of DDT cancellation. The use of these compounds is most extensive in the south-

metabolites of phorate in blood after oral administration to rats have been shown to be phorate sulfoxide and phoratoxon sulfone.

Disulfoton follows essentially the same metabolic routes as phorate. Initial rapid conversion to the sulfoxide is followed by oxidation to the sulfone and oxidative desulfuration to the disulfotoxon sulfoxide and sulfone. Hydrolysis competes with the oxidative process to form the various phosphoric acids (Bull, 1965). Metabolism of disulfoton in plants parallels that in mammals. The oxidative metabolites are formed first, followed by hydrolysis to phosphoric acids.

Health Aspects

Observations in Man

EPA accident files contain reports of 21 episodes of poisoning involving phorate for the period 1971–1973. Eleven were classified as agricultural, six as industrial, and four as having other causes. There have been no fatalities from phorate poisoning. There are no controlled studies of phorate in humans from which no-adverse-effect dosages could be derived.

Five human subjects were given disulfoton at 0.75 mg/kg for 30 days. Measurement of plasma and red-cell cholinesterase during the administration period and for 30 days thereafter showed no decrease in cholinesterase (Rider *et al.*, 1972).

Observations in Other Species

Acute Effects Both disulfoton and phorate have high acute toxicity in laboratory animals. The oral LD_{50} of phorate in rats is reported variously as 1.75 mg/kg (Hazleton, 1953); 2.71-4.11 mg/kg (Tusing, 1955); and 17.7 mg/kg (American Cyanamid, 1966; cited in USEPA, 1974e). The oral LD_{50} of disulfoton in male rats is reported variously as 12.5 mg/kg (Bombinski and DuBois, 1958; Wysocka-Paruszewska, 1970) and 6.8 mg/kg (Gaines, 1969) and in female rats as 2.6 mg/kg (Wysocka-Paruszewska, 1970; Bombinski and DuBois, 1958), 2.3 mg/kg (Gaines, 1969), and 2.8 mg/kg (McPhillips and Dar, 1967). Studies on the acute oral toxicity of phorate in other animals were not found. The acute oral LD_{50} of disulfoton in mice and guinea pigs are about the same as those in rats (Bombinski and DuBois, 1958; Stevens *et al.*, 1972).

Studies to determine the acute dermal LD_{50} of phorate gave values of 3 mg/kg in rats (Shaffer, 1958), 20 mg/kg in male guinea pigs (American Cyanamid, 1966; cited in USEPA, 1974e), and 71 mg/kg in rabbits

performance was 1.5 ppm (American Cyanamid, 1965b; cited in USEPA, 1974e).

There are no published studies on the effects of disulfoton on reproduction.

Teratogenicity No teratogenicity studies of phorate have been reported. However, in the studies on reproductive performance reported above, no abnormalities, including skeletal changes, could be related to phorate administration. Phorate was also studied in the chick embryo test (Richert and Prahlad, 1972). Phorate in peanut oil was injected into eggs on the tenth day of incubation at 1.5 or 2.0 ppm. Controls received peanut oil only. Hatchability of the eggs was decreased in a dose-dependent manner. Malformations were produced, but these did not seem to be dose-related. The relevance of these studies to mammalian teratology is unclear.

There are no published reports of teratogenicity studies of disulfoton.

Conclusions and Recommendations

Phorate and disulfoton are widely used agricultural insecticides. They are organophosphorus compounds whose mode of action, inhibition of acetylcholinesterase, is well understood. Both have high acute toxicity in laboratory animals. Because of this and a known mode of action, studies on the possible chronic toxicity of these compounds have been neglected. There is very little toxicologic research on disulfoton reported in the open literature. There is a single subchronic-toxicity study, in which no adverse effects were observed after administration of 0.75 mg/kg/day for 30 days; this indicates that disulfoton would pose less hazard than phorate. Based on subchronic toxicity data, an ADI was calculated at 0.0001 mg/kg/day for both phorate and disulfoton. The available data and calculations of ADI are summarized in Table VI-31.

Phorate and disulfoton are converted in the environment and in mammalian systems to a series of highly toxic oxidative metabolites, which are known to be more potent cholinesterase inhibitors than the parent compounds (Curry *et al.*, 1961). These materials must be considered when evaluating the toxicity of phorate and disulfoton. Therefore, it is proposed that the derived no-adverse-effect dosages of these compounds be considered to include their oxidative metabolites as well.

Sensitive methods for analyzing residues of phorate and disulfoton are available. A gas-liquid chromatographic method is available that can detect 0.01 ppm in milk; and a cholinesterase-inhibition method can